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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,453	03/20/2001	R. Rogers Yocum	OGZ-001	3274

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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/813,453	YOCUM ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-25 and 37* is/are pending in the application.

4a) Of the above claim(s) *15 and 17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 March 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *13* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and subgroup 6 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that there is no undue burden on the examiner in searching the different inventions. The applicant presents two arguments that examination of all the claimed inventions in this application would not present an undue burden. First, Applicant argues that the existence of a linking claim demonstrates that there is a unifying concept that links the various inventions, and thereby demonstrates that there would be no serious burden in searching the linked inventions. The Applicant also argues that the common classification of the various groups further demonstrates that there would be no burden in the examination, as the searches would have substantial overlap. These arguments are not found persuasive.

The arguments are not found persuasive because, although there may be an allowable linking concept, in the interim the examiner would be forced to search each of the various claimed methods. As the various methods perform the same function (identify antibiotics), they do so through different processes, albeit involving related products. However, because it is the methods that are to be searched, and because a search for any one of these methods would not be coextensive with searches for the other methods, there is a burden in the examination of the various methods. The common classification is not an indication that the different methods would be fully searched by a consideration of the art relevant to any one of the claimed inventions. Further, while the linking claim will be considered along with the elected method, unless such claim has been found allowable (thereby indicating that all inventions linked by that

claim are also allowable), the existence of the claim does not demonstrate that the searches for the various methods it comprises would be coextensive and not burdensome.

With regards to the restriction among Group I1-I33, the restriction is not a species election as each of these inventions comprises a method using a different protein, isolated from a different organism, and encoded by a different DNA sequence. The Applicant's argument that the different inventions are patentably distinct is not understood as this supports the Examiners restriction among the proteins. As the applicant has provided no rational as to why the inventions should be considered species, and not separate inventions, the argument is not found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

The applicant's further election of Group VII2 is noted, but, as this election was not required (in view of applicant's election of Group I), it has no bearing on the claims currently under examination. See, Restriction, page 4 (indicating that election of one of Groups VII1 and VII2 is required only if Group VII was elected).

The Examiner hereby rejoins the inventions of Groups I-III and the Examiner does not believe that there is a burden in the search of these inventions. Thus, the pending claims under consideration are claims 1-14, and 37. These claims will be considered to the extent that they read on methods of identifying antibiotics using the protein of SEQ ID NOs: 2, 14/67, and 20 (the restriction to the two sequences other than SEQ ID NO: 2 being hereby withdrawn).

2. Claims 13-15, and 19-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Sequence Listing

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. It is noted that, the paper copy of the sequence listing lists certain sequence identification numbers two times, with different sequences attached thereto. This can be seen in the paper copy of the sequence listing starting at page 61 (listing several identifies starting with SEQ ID NO: 70 for the second time). Corrected copies of the paper sequence listing, and an updated copy of the CRF (if necessary) is required.

Applicant is given three months from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on May 9, 2003 in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Drawings

5. New corrected drawings are required in this application because the sequence identification numbers associated with the various bacterial proteins in Figure 6 do not appear to match the bacterial species given for those sequence identifiers in the sequence listing. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying antibiotics by identifying compounds that reduce the activity of pantothenate kinase, does not reasonably provide enablement for such methods by identifying compounds that either bind to (no affect on activity) or increase pantothenate kinase

activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims describe methods of identifying antibiotics by identifying compounds that either bind to or modulate the activity of pantothenate kinase. To modulate the activity of the While it is accepted in the art that pantothenate kinase activities are necessary to bacterial life, the art does not indicate, or the specification teach, that an increase in the activity of the protein would be harmful to the bacterial cell, thus an effective antibiotic. Therefore, while the Applicant is enabled for methods of identifying antibiotic compounds by identifying compounds that reduce the activity of the protein, the applicant is not enabled for methods of identifying antibiotics whereby the identified compound merely binds, or increases the activity of the pantothenate kinase.

7. Claims 37, and 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make, and/or use the invention. These claims have been identified above. Claims 9 and 10 identify a number of specific protein sequences that the Applicant identifies as CoaX proteins. However, as can be seen in the attached sequence search results, the relationship among these sequences ranges from 90% matches down to single digit percent identities among the various proteins. Thus, the claims read on a wide array of proteins, some of which may be recognized as related, and others which do not appear to be so related (see

e.g. the search results of the proteins of SEQ ID NOs: 53, 11, 41, and 15, none of which share 25% or more sequence identity with any of the other proteins, including each other).

The Applicants have provided in the application a sequence comparison of several proteins. App., Figure 6. However, while the Applicant has shown some somewhat conserved regions among some of the proteins, there is not clearly preserved sequence of motif that one in the art would recognize as potentially identifying a family of proteins, or at least a family that includes all of the identified sequences. Thus, the application appears to rely solely on sequence homology to identify CoaX proteins (in that pantothenate kinase activity has been shown for only 3 proteins, page 45). The art, however, does not recognize that sequence homology is sufficient for identifying the function of proteins. See e.g., Skolnick et al., Trends in Biotech 18(1): 34-39 (2000); and Bork et al., Genome Research 10: 398-4000 (2000) (each describing the uncertainty in predicting protein function fro its structure). See also, Scott et al., Nature Genetics 21: 440-43 (April 1999, demonstrating an instance of misidentification of protein function due to reliance on protein sequence homology). The Applicant has not shown that all of the identified proteins are indeed pantothenate kinases, or provided sufficient guidance such that one skilled in the art could identify any or all such proteins without undue experimentation to determine whether any particular bacterial protein is actually a pantothenate kinase, and therefore possibly a Coax protein.

Further, while most proteins share at least an approximately equal protein length, three proteins, those of SEQ ID NOs: 43, 22, and 39 each have either 460 or 592 amino residues in their sequences. These three proteins share a relatively high percent identity amongst themselves, but none of them shares greater than 15% identity with any of the other identified proteins. Nor

does the application establish that these proteins have a pantothenate kinase activity. In view of the above, and the lack of identity between these proteins and the other identified proteins, the Applicant has not shown that these proteins are pantothenate kinases, or that if they do have this activity, that they would be considered part of the same gene family as the remainder of the proteins.

Because the application does not show any conserved motif or defined active region among the disclosed proteins, and in view of the significant variations in homology seen among the proteins, and the fact that only 3 of the proteins have been shown to have the claimed activity, the application has not enabled those in the art to practice the claimed invention because the Applicant has not adequately defined the claimed subset of pantothenate kinases referred to as Coax proteins. Because those in the art have not been enabled to identify the CoaX pantothenate kinases, the Applicant is not enabled in the use of any CoaX protein for the identification of an antibiotic.

8. Claims 37, and 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. The claims are rejected because the Applicant has not demonstrated that they are in possession of the claimed genus of proteins referred to as CoaX proteins.

> The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35

U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the Applicant has provided a number of examples of proteins that they identify as Coax proteins. However, as described above, the applicant has not demonstrated that all of the proteins so identified are actually members of the claimed genus. Aside from providing a list of potential CoaX proteins, the Applicant has not identified any structural feature that identifies a CoaX protein, other than that these proteins are encoded by genes that are structurally distinct from other pantothenate kinase genes. Page 9. However, the application has not established that the identified proteins each have the Coax pantothenate kinase activity, or identified any conserved structure or motif by which one of ordinary skill in the art could distinguish CoaX proteins from other pantothenate kinases. Thus, the application does not adequately describe a genus of proteins that can be classified as CoaX proteins.

Furtherer, the applicant appears to be claiming any pantothenate kinase other than those encoded by the coaA gene. As the applicant has identified only one further subset of

pantothenate kinases (those related to SEQ ID NOs: 2, 14, and 20), the applicant is not entitled to claims that read on methods of identifying antibiotics using any CoaX protein as defined by the Applicant. The application therefore does not provide adequate written description for the genus of proteins used in the claimed method.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-14, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been identified above. They read on a method of identifying antibiotics by identifying molecules that inhibit the pantothenate kinase activity of CoaX proteins. However, while the Applicant has provided a number of examples of putative CoaX pantothenate kinases, the applicant has not provided a means by which those skilled in the art can distinguish CoaX pantothenate kinases from other proteins.

While there is a functional requirement, the applicant has not identified a structure associated with the identified genus of proteins. For example, the specification provides a sequence alignment of a number of proteins, but does not identify any regions or motifs that are essential to the protein function, or that identify a particular pantothenate kinase as a CoaX protein. Further, the specification describes a Coax protein as a protein encoded by the CoaX gene. Pages 2 and 17. CoaX genes are defined as novel microbial pantothenate kinase encoding genes that are distinct from the coaA gene. Page 9. However, there is no structural identification

of this family of genes (as opposed to the individual genes identified as members of the family), other than that they are "structurally distinct from a previously identified microbial pantothenate kinase encoding gene, coaA." Page 9. In view of the lack of a identified structure by which one skilled in the art could identify a member of this group, and the lack of a correlation between the protein families' assigned function and such a structure, one skilled in the art would not, from the present disclosure, be able to determine if a particular protein with a pantothenate kinase activity was, or was not, a member of the CoaX protein genus. The claims are therefore indefinite.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 37 is rejected under 35 U.S.C. 102(e) as being anticipated by Dougherty et al., WO 01/49721. This claim describes a method of identifying an antibiotic by identifying modulators of pantothenate kinase. Dougherty teaches the identification of antibacterial compounds by identifying compounds that disrupt the function of a class of bacterial proteins identified as conserved essential gene (CEG) proteins. Pages 3, and 64. Among the proteins identified as CEG proteins is pantothenate kinase. Page, 41. Thus, the reference teaches the

identification of antibacterial compounds (antibiotics) by identifying compounds that disrupt (modulate) pantothenate kinase activity. The reference therefore anticipates the identified claims.

Conclusion

13. No claims are allowed. The embodiments reading on methods of using the proteins of SEQ ID NOs: 2, 14/67 (the same protein), and 20 appear to be allowable over the prior art.

14. It is noted that the Examiner had indicated in an earlier interview that the claims would be in condition for allowance if claim 37 was amended to include all of the limitations of claim 1. However, upon further review, and in view of the above rejections, the Examiner has concluded that this assessment of the claims was in error.

15. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

U.S. Patent Application Publication 2002/0160456, naming Kleanthous et al. as inventors. This reference teaches a series of proteins from bacteria of the genus Helicobacter identified as potential vaccines against Helicobacter infections. Page 3, sentence spanning left and right columns. Among the proteins disclosed therein is SEQ ID NO: 74, which is a 100% match for the sequence identified as SEQ ID NO: 14 (and as SEQ ID NO: 67) in the present application. However, the reference does not teach the function of this protein, or that it may be used in a method to identify antibiotics.

U.S. Patent Application Publication 2002/0164588, naming Eisenberg et al. as inventors. This reference teaches a method of identifying bacterial genes and proteins that are potential targets of anti-bacterial drugs. Abstract. Among the proteins so identified in the reference is SEQ ID NO: 74, which shares 99.7% homology with SEQ ID NO: 5 of the present application. However, the reference neither positively identifies the protein as

such a drug target, nor identifies the function of the protein. Thus, the reference does not enable one of ordinary skill in the art to practice the presently claimed invention.

DeShazer et al., J Bacteriol 177(13) : 3801-07. This reference teaches that the B. pertussis baf protein (SEQ ID NO: 15 in the present application) is an essential protein to that bacterium. By indicating this, the reference teaches that this protein may be an antibacterial drug target. However, the reference does not teach that the function of the protein. Thus, it does not teach a method of identifying compounds that inhibits its pantothenate kinase activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
June 30, 2003

James C. Housel 6/30/03

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